

105. (New) The gene construct of claim 101 wherein the inverted repeat sequence comprises an intervening sequence between the sequence of at least 25 nucleotides and the sequence complementary thereto.
106. (New) The transgenic cotton plant of claim 70, wherein the seed oil from said plant comprises 58.5% oleic acid.
107. (New) The transgenic cotton plant of claim 106, wherein the seed oil from said plant comprises 66.0% oleic acid.
108. (New) The transgenic cotton plant of claim 106, wherein the seed oil from said plant comprises 68.9% oleic acid.

REMARKS

Claims 1-61 have been canceled without prejudice, and new claims 62-108 have been presented. The new claims are supported by the as-filed claims and by the as-filed Specification. The recitation of at least 20 nucleotides is supported in the as-filed Specification at page 38, lines 21-28. The recitation of particular percent oleic acid contents (new claims 106-108) is supported by Table 10. Details of the relationships of as-filed and new claims, at least in part, are provided in the table submitted with this response.

In view of the foregoing, none of the amendments made herein constitutes the addition of new matter.

The Requirement for Restriction

The Patent Office has required restriction under 35 U.S.C. 121, alleging that the claims as filed embodied twenty-nine separately patentable inventions. Applicants respectfully traverse the requirement for restriction, as set forth below.

- I. Claims 1-3, 8, 10-16, 18-23, method of modifying the endogenous oil content of cotton comprising transforming a plant with a coding sequence of a fatty acid $\Delta 9$ desaturase and the plants transformed therewith, Class 800, subclass 281.
- II. Claims 1-3, 8, 10-16, 18-23, to the extent that the claims are drawn to a method of modifying the endogenous oil content of cotton comprising transforming a plant with a complement or antisense of a fatty acid $\Delta 9$ desaturase and the plants transformed therewith, Class 800, subclass 281.
- III. Claims 1, 2, 4, 8, 10-15, 17-23 to the extent that the claims are drawn to a method of modifying the endogenous oil content of cotton comprising transforming a plant with inverted repeats of a fatty acid $\Delta 9$ desaturase and the plants transformed therewith, Class 800, subclass 281.
- IV. Claims 1-3, 8, 10-16, 18-23, method of modifying the endogenous oil content of cotton comprising transforming a plant with a coding sequence of a fatty acid $\Delta 12$ desaturase and the plants transformed therewith, Class 800, subclass 281.
- V. Claims 1-3, 8-16, 18-23, to the extent that the claims are drawn to a method of modifying the endogenous oil content of cotton comprising transforming a plant with a complement or antisense of a fatty acid $\Delta 12$ desaturase and the plants transformed therewith, Class 800, subclass 281.
- VI. Claims 1, 2, 4, 8, 10-15, 17-23 to the extent that the claims are drawn to a method of modifying the endogenous oil content of cotton comprising transforming a plant with inverted repeats of a fatty acid $\Delta 12$ desaturase and the plants transformed therewith, Class 800, subclass 281.
- VII. Claims 5, 6, 24-25, 27-35 to the extent the claims are drawn to a method of modifying the endogenous oil content of cotton comprising transforming a plant with a fatty acid biosynthesis gene and the plants transformed therewith, Class 800, subclass 281.

- VIII. Claims 5, 6, 24-25, 27-35, to the extent that the claims are drawn to a method of modifying the endogenous oil content of cotton comprising transforming a plant with a complement or antisense of a fatty acid biosynthesis gene and the plants transformed therewith, Class 800, subclass 281.
- IX. Claims 5, 7, 24, 26-35 to the extent that the claims are drawn to a method of modifying the endogenous oil content of cotton comprising transforming a plant with inverted repeats of a fatty acid biosynthesis gene and the plants transformed therewith, Class 800, subclass 281. The Examiner has indicated that if this group is elected for examination, then one of SEQ ID NO:3, 4 and 7 must also be elected.
- X. Claim 36 to the extent that the claims are drawn to a method of modifying the endogenous oil content of cotton comprising transforming a plant with a coding sequence of a fatty acid $\Delta 9$ desaturase and with a coding sequence of a fatty acid $\Delta 12$ desaturase and the plants transformed therewith, Class 800, subclass 281.
- XI. Claim 37 to the extent that the claims are drawn to a method of modifying the endogenous oil of cotton comprising transforming a plant with a fatty acid biosynthesis gene and a second gene, and the plants transformed therewith, Class 800, subclass 281, for example. The Examiner has indicated that if this group is elected for examination, then one of SEQ ID NO:3, 4 and 7 must also be elected.
- XII. Claims 38-45 to the extent that the claims are drawn to a method of modifying the endogenous oil of cotton comprising transforming a plant with fatty acid delta-9 desaturase gene, transforming a second plant with a fatty acid delta-12 desaturase gene, and crossing the two plants to produce progeny plants, classified in Class 800, subclass 264.
- XIII. Claims 46-48 drawn to a cotton plant with modified fatty acid composition, classified in Class 800, subclass 314.
- XIV. Claims 49-52 drawn to cottonseed oil, classified in Class 426, subclass 601.

- XV. Claims 53, 54 and 56 to the extent that the claims are drawn to a gene construct comprising SEQ ID NO:1 or a sequence encoding SEQ ID NO:____, [sic] classified in Class 536, subclass 23.1.
- XVI. Claims 53, 54 and 56 to the extent that the claims are drawn to a gene construct comprising SEQ ID NO:3, classified in Class 536, subclass 23.1.
- XVII. Claims 53 and 56 to the extent that the claims are drawn to a gene construct comprising SEQ ID NO:7, classified in Class 536, subclass 23.1.
- XVIII. Claims 53 and 56 to the extent that the claims are drawn to a gene construct comprising SEQ ID NO:4, classified in Class 536, subclass 23.1.
- XIX. Claims 53, 54 and 56 to the extent that the claims are drawn to a gene construct comprising the complement of SEQ ID NO:1 or a sequence encoding SEQ ID NO:2, classified in Class 536, subclass 23.1.
- XX. Claims 53, 54 and 56 to the extent that the claims are drawn to a gene construct comprising the complement to SEQ ID NO:3, classified in Class 536, subclass 23.1.
- XXI. Claims 53 and 56 to the extent that the claims are drawn to a gene construct comprising the complement to SEQ ID NO:7, classified in Class 536, subclass 23.1.
- XXII. Claims 53 and 56 to the extent that the claims are drawn to a gene construct comprising the complement to SEQ ID NO:4, classified in Class 526, subclass 23.1.
- XXIII. Claims 53, 55 and 56 to the extent that the claims are drawn to a gene construct comprising inverted repeats, classified in Class 536, subclass 23.1.
- XXIV. Claim 57 to the extent that the claims are drawn to a method of modifying the endogenous oil of cotton comprising transforming a plant with a coding sequence of a fatty acid delta-9

desaturase gene, wherein inverted repeats are interrupted by an intervening sequence, classified in Class 800, subclass 281.

- XXV. Claim 57 to the extent that the claims are drawn to a method of modifying the endogenous oil of cotton comprising transforming a plant with a coding sequence of a fatty acid delta-12 desaturase gene, wherein inverted repeats are interrupted by an intervening sequence, classified in Class 800, subclass 281.
- XXVI. Claim 58 to the extent that the claims are drawn to a method of modifying the endogenous oil of cotton comprising transforming a plant with a fatty acid biosynthesis gene, wherein inverted repeats are interrupted by an intervening sequence, classified in Class 800, subclass 281.
- XXVII. Claim 59 to the extent that the claims are drawn to a method of modifying the endogenous oil of cotton comprising transforming a plant with SEQ ID NO:1, wherein inverted repeats are interrupted by an intervening sequence, classified in Class 800, subclass 281.
- XXVIII. Claim 60 to the extent that the claims are drawn to a method of modifying the endogenous oil of cotton comprising transforming a plant with a fatty acid biosynthesis gene, wherein inverted repeats are interrupted by an intervening sequence, classified in Class 800, subclass 281.
- XXIX. Claim 61 to the extent that the claims are drawn to a method of modifying the endogenous oil of cotton comprising transforming a plant with a fatty acid biosynthesis gene, wherein inverted repeats are interrupted by an intervening sequence, classified in Class 800, subclass 281.

Applicants provisionally elect with traverse the claims of Group VI, claims 1, 2, 4, 8, 10-15, 17-23 to the extent that the claims are drawn to a method of modifying the endogenous oil content of cotton comprising transforming a plant with inverted repeats of a fatty acid Δ 12 desaturase. The Examiner has not specifically required the election of a particular nucleotide sequence of a fatty acid Δ 12 desaturase coding sequence or gene. New claims 62, 68, 70-74 correspond directly to as-filed claims 1, 8 and 10-14

within this group, but all the newly presented claims read on the elected group. However, in keeping with the common mechanism of action of the sequences regulating gene expression, as discussed in depth below, Applicants have provided amended claims which, in the broadest sense, recite the use of gene constructs comprising at least 20 nucleotides of a fatty acid $\Delta 12$ desaturase gene.

Applicants respectfully maintain that Groups IV, V, VI and Groups VII, VIII, IX should be rejoined because they all relate to nucleic acids encoding fatty acid $\Delta 12$ desaturase of cotton. Groups IV, V and VI recite particular nucleic acid sequences while Groups VII, VII and IX relate to nucleic acid sequences encoding a specifically exemplified fatty acid $\Delta 12$ desaturase amino acid sequence. SEQ ID NOs:3, 4 and 7 all relate to sequences of a particular fatty acid $\Delta 12$ desaturase gene. SEQ ID NO:4 is the encoded amino acid sequence related to SEQ ID NO:3 (nucleotide sequence). See page 25. SEQ ID NO:7 comprises the 5' untranslated region of the gene corresponding to the coding sequence embodied in SEQ ID NO:3. Furthermore, SEQ ID NO:7 is at least partially overlapping with SEQ ID NO: 3, as described on page 10, lines 11-15. In particular, SEQ ID NO:7 includes the entire 5'-untranslated region of the ghFAD2-1 gene. Accordingly, Applicants respectfully submit that it is appropriate to examine claims reciting these sequences together as these three sequences are all associated with the ghFAD2-1 gene.

In addition, the rejoinder of the claims of Group XXIV-XXVIII together with those elected is respectfully requested. These claims are drawn to the use of inverted repeats of sequences encoding fatty acid $\Delta 12$ desaturase, where the repeats are interrupted by an intervening sequence. Applicants respectfully submit that the presence of an intervening sequence does not change the mechanism by which the fatty acid $\Delta 12$ desaturase-derived sequences act to regulate gene expression and oil content of cotton seeds, and thus, these claims should be examined with the remaining claims groups. Applicants also note that the claims within Groups XXIV-XXVIII have the same sequence relationships of coding sequences as do the claims of Groups IV-VIII, as discussed in the previous paragraph.

The rejoinder of Groups IV, V and VI should be allowed because of the common mechanism by which gene expression is regulated in the context of antisense, co-suppression and the use of inverted repeats. Applicants respectfully submit that there is a basic similarity in the mechanisms by which gene silencing is accomplished using antisense, sense and inverted repeat-mediated expression, as evidenced by the publications submitted herewith and discussed below:

Bruening, G. (1998) "Commentary: Plant gene silencing regularized," Proc. Natl. Acad. Sci. USA 95: 13349-13351 discusses advances made in the area of cosuppression/gene silencing and antisense suppression. He raises the question "are antisense suppression and sense RNA-mediated PTGS (post-transcriptional gene silencing) related phenomena, in at least some instance?" and answers this question with "The stringent sequence specificity, exhibited by both phenomena suggests that this is the case" (p. 13350, col. 1). He further states "These results suggest a common intermediate for antisense RNA-mediated and sense RNA-mediated gene silencing. Logically, this intermediate would be double-stranded RNA." (p. 13350, col. 1). This reference is submitted herewith as Exhibit A.

Stam et al. (2000) "Distinct features of post-transcriptional gene silencing by antisense transgenes in single copy and inverted T-DNA repeat loci," Plant J. 21: 27-42 provides experimental evidence that antisense and sense-mediated gene suppression work by the same post-transcriptional gene silencing mechanism when strong gene suppression occurs. With regard to antisense suppression, this paper states "we speculate that silencing is induced by double-stranded RNA" and "Similar features have been described for cosuppression by IRS composed of sense *Chs* transgenes, suggesting that silencing by antisense IRs also occurs by cosuppression" (p. 27, abstract), and "The similarities with IR silencing loci containing sense-transgenes suggest that silencing by as (antisense)-transgene IR loci is mechanistically similar to that by sense-transgene IR loci" (p. 28, col. 1). These authors conclude "It is therefore attractive to propose that antisense inhibition, in particular by IRs, is identical to cosuppression by sense transgenes" (p. 39, col. 1). A copy of this reference is submitted herewith as Exhibit B.

Waterhouse et al. (2001) "Gene silencing as an adaptive defense against viruses," Nature 411: 834-842 provides a review of the mechanism of gene silencing in plants, and relates it to the corresponding mechanism in mammals, other animals and fungi. This reference, submitted herewith as Exhibit C, clearly points out that the inducer of the silencing system is double-stranded RNA which is produced either from an antisense or a sense transgene with the aid of RNA dependent RNA polymerase or from an inverted repeat (sense + antisense) transgene.

Van Houdt et al. (2000) "Both sense and antisense RNAs are targets for the sense transgene-induced posttranscriptional silencing mechanism," Molecular and General Genetics 263:995-1002 reports that both sense and antisense RNAs are recognized and degraded by the same mechanism. A copy of this reference is provided as Exhibit D.

Because of the common mechanisms with respect to gene silencing by sense, antisense and inverted repeats, including those inverted repeats interrupted by an intervening sequence, Applicants respectfully urge that the Patent Office rejoin the relevant claims of Groups IV and V, as drawn to sequences derived from a fatty acid $\Delta 12$ desaturase coding sequence. Applicants respectfully submit that claim 62 is a linking claim. The common technical feature of the claims is the construct derived from a fatty acid desaturase as a mechanism to regulate fatty acid content of cotton seeds. However, Applicants make no admission that any claim or claims is/are obvious over any other claim. To the extent that it is necessary to elect a

specific sequence, Applicants elect the nucleotide sequences encoding a protein consisting of the amino acid sequence given in SEQ ID NO:4. Applicants respectfully note that SEQ ID NO:3 is a species within the nucleotide sequences embodied by nucleic acids encoding a protein having the nucleotide sequence of SEQ ID NO:4 and thus reads on the elected species. Claims reading on the elected sequence include all the newly presented claims. In addition, the Patent Office has separated out the claims that refer to an inverted repeat interrupted by an intervening sequence (Claims 57-61, Groups XXIV to XXVIII) from the other inverted repeat claims (Groups III, VI, IX). However, a construct comprising an inverted repeat with an intervening sequence is clearly a subset of constructs comprising inverted repeats. That is, the technical feature in common is the inverted repeat. Taking a step further back, a broader division is a construct comprising all or a portion of the desaturase coding or upstream sequence. The recitation of inverted repeats provides a limitation of the type of sequence embodied within the construct.

The Patent Office has further separated the claims that refer to a combination of $\Delta 12$ -desaturase genes and $\Delta 9$ -desaturase genes (Claims 36-48, Groups X, XI, XIII) from the claims that refers only to use of one of these genes. However, use of "genes A and B together" is a subset of use of "gene A". Rejoinder of these claims with those of the group provisionally elected is respectfully requested.

Further, Applicants respectfully request that the "gene construct" claims (Groups XV - XXIII) be reunited with the claims that refer to the methods of using them, and to the plants comprising them. These claims all have the unifying technical concept of regulation of fatty acid content of cotton seed.

As a further matter, Applicants respectfully note that the Examiner appears to have omitted any reference or commentary relative to the use of fragments derived from the sequences useful in the practice of the present invention. Page 23-24 defines "gene fragment" in general terms. The paragraph beginning at page 27, lines 24, describes preferred gene fragments as comprising at least about 50 nucleotides derived from the full-length gene sequence. (Note that an inverted repeat of 25 + 25 nucleotides actually includes 50 nucleotides from the gene sequence when considering the double-stranded DNA of the gene). The Specification at page 37-38 describes the inverted repeat type of construct as using gene fragments of only 25 nucleotides in length or longer. (This paragraph is in the context of inverted repeats). Page 38, lines 22-28, describes the minimum size as at least about 10-20 nucleotides of the target gene, in the context of either antisense or PTGS (inverted repeat).

Applicants respectfully note that claims 3, 4, 16 and 17 relate to SEQ ID NO:1 which is the nucleotide sequence for a fatty acid $\Delta 9$ desaturase gene yet have been included in Groups IV, V and/or VI which relate only to a fatty acid $\Delta 12$ desaturase, and request consideration of the appropriate groupings with respect to these claims. It appears there has been an error in the characterization and grouping of the claims in the context of the restriction requirement.

Applicants respectfully submit that claim 8 should have been put into Groups VII, VIII and IX as well. It depends from claim 1 and adds limitations with respect to the nature of the promoter driving expressing of the desaturase-derived construct.

Applicants respectfully submit that claim 9 should also have been put into Groups I, III, IV and VI, as it relates to sense and inverted repeats just as much as it does to antisense.

Applicants respectfully suggest that claim 24 and dependent claims should have been included in Groups I – VI, for the reason mentioned above with respect to claim 8.

Applicants respectfully maintain that as-filed claim 24 and claims dependent thereon should be reunited with those of Group VI. Note that the as-filed transgenic plant claims (Claims 27-35) depend from claim 24. Although the Examiner has stated that Group VI includes "the plants transformed therewith," she has not specifically recited any claims directed to the cotton plants in this Group.

In view of the errors set forth in the requirement for restriction, the clarifying statements, arguments and requests presented above, and the amended claims to be entered, Applicants respectfully request reconsideration of the requirement for restriction and regrouping of the claims accordingly. The division of the present invention as claimed into twenty nine claims groups is neither reasonable nor fair to Applicants. Furthermore, Applicants respectfully urge that all the nucleic acid sequences, specifically or as synonymous codings of specified amino acid sequences could be searched without placing an undue burden on the Patent Office, as up to 10 sequences can be searched within an application.

Conclusion

In view of the foregoing, it is submitted that this case is in condition for allowance, and passage to issuance is respectfully requested.

If there are any outstanding issues related to patentability, the courtesy of a telephone interview is requested, and the Examiner is invited to call to arrange a mutually convenient time.

This response is accompanied by a Petition for Extension of Time (three months) and a check in the amount of \$930.00 (large entity) for the fee required under 37 C.F.R. 1.17. It is believed that no other fees are required. If the enclosed amount submitted is incorrect, please deduct any deficiency or credit any overpayment to Deposit Account No. 07-1969.

Respectfully submitted,



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SCHEDULE

| New Claim | Old Claim | Additional Support |
|---------------|-----------|-------------------------------------|
| 62 | 1 | p.23 lines 19-28; p.38 lines 22-26 |
| 63 | 5 | p.25 line 15 - p.26 line 7. |
| 64 | 5, 53 | p.37 line 13 – p.38 line 8. |
| 65 | 7, 53 | p.37 line 13 – p.38 line 8. |
| 66 | 7 | p.37 line 13 – p.38 line 8. |
| 67 | 6 | p.23 lines 19-28; p.38 lines 22-26. |
| 68 | 8 | |
| 69 | 9 | |
| 70 | 10 | |
| 71 | 11 | |
| 72 | 12 | |
| 73 | 13 | |
| 74 | 14 | p.23 lines 19-28; p.38 lines 22-26. |
| 75, 76 | 24 | p.37 line 13 – p.38 line 8. |
| 77, 78 | 26 | p.37 line 13 – p.38 line 8. |
| 79 | 25 | |
| 80 | 28 | |
| 81 | 27 | |
| 82 | 31 | |
| 83 | 30 | |
| 84 | 33 | |
| 85 | 34 | |
| 86, 87 | 37 | p.23 lines 19-28; p.38 lines 22-26. |
| 88 | 38 | |
| 89 | New | |
| 90 | 40 | |
| 91 | 39 | |
| 92 | New | |
| 93 | 41 | |
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| 96 | 44 | |
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| 99 | 47 | |
| 100 | 48 | |
| 101 | 53, 55 | p.37 line 13 – p.38 line 8. |
| 102 | 56 | |
| 103 | 58 | p.37 line 13 – p.38 line 8 |
| 104 | 60 | |
| 105 | 61 | |
| 106, 107, 108 | New | pp.111-112; Table 10. |